

THE CLAIMS

1. A vector delivery structure comprising:
 - a) a cochleate comprising a lipid bilayer element and cations;
 - b) one or more proteins that facilitate the integration of one or more therapeutic nucleotide sequences into the genome of a host cell; and
 - c) a polynucleotide comprising one or more DNA sequences recognized by the one or more proteins and one or more oligonucleotides or polynucleotides, each containing a therapeutic nucleotide sequence that expresses a therapeutically beneficial molecule.
2. The vector delivery structure of claim 1, wherein the polynucleotide is selected from the group consisting of a plasmid or nucleic acid construct.
3. The vector delivery structure of claim 1, wherein the structure does not include a polynucleotide that expresses one or more proteins that facilitate integration.
4. The vector delivery structure of claim 1, wherein the cation is a divalent cation
5. The vector delivery structure of claim 1, wherein the cation is calcium.
6. The vector delivery structure of claim 1, wherein the one or more proteins that facilitate the integration of one or more therapeutic nucleotide sequences into the genome of a host cell is a binding protein that has a DNA binding function.
7. The vector delivery structure of claim 5, wherein the one or more binding proteins are from adeno-associated virus type II.
8. The vector delivery structure of claim 6, wherein the one or more binding proteins are at least one adeno-associated virus protein selected from the group consisting of Rep 68 and Rep 78.
9. The vector delivery structure of claim 6, wherein the one or more binding

proteins comprise with Rep 68 and Rep 78.

10. The vector delivery structure of claim 1, 8 or 9, wherein the one or more DNA sequences recognized by the one or more binding proteins are the inverted terminal repeat regions of adeno-associated virus.

11. The vector delivery structure of claim 10, wherein the one or more oligonucleotides or polynucleotides comprise a length of DNA that is flanked at each end by at least one of the inverted terminal repeat regions.

12. The vector delivery structure of claim 6, wherein at least one of the one or more binding proteins is an integrase and at least one of the one or more DNA sequences recognized by the one or more binding proteins is a substrate for said integrase.

13. The vector delivery structure of claim 12, wherein at least one of the one or more binding proteins is an integrase that is not Rep 68 or Rep 78.

14. The vector delivery structure of claim 6, wherein at least one of the one or more binding proteins is a helicase and at least one of the one or more sequences recognized by the one or more DNA binding proteins is a substrate for said helicase.

15. The vector delivery structure of claim 6, wherein at least one of the one or more binding proteins is a DNA excision enzyme and at least one of the one or more DNA sequences recognized by the one or more binding proteins is a substrate for said DNA excision enzyme.

16. The vector delivery structure of claim 6, wherein at least one of the one or more binding proteins is an isomerase and at least one of the one or more DNA sequences recognized by the one or more binding proteins is a substrate for said isomerase.

17. The vector delivery structure of claim 6, wherein at least one of the one or more binding proteins is a telomerase and at least one of the one or more DNA sequences recognized by the one or more binding proteins is a substrate for said telomerase.

18. The vector delivery structure of claim 6, wherein at least one of the one or more

binding proteins is a DNA repair enzyme and at least one of the one or more DNA sequences recognized by the one or more binding proteins is a substrate for said DNA repair enzyme.

19. The vector delivery structure of claim 1, wherein at least one of the one or more proteins that facilitate the integration of the one or more therapeutic nucleotide sequences into the genome of the host cell is a protein that has gene regulatory activity and at least one of the one or more DNA sequences recognized by the one or more binding proteins is a substrate for said protein that has gene regulatory activity.

20. The vector delivery structure of claim 1, wherein at least one of the one or more proteins that facilitate the integration of the one or more therapeutic nucleotide sequences into the genome of the host cell is a protein that facilitates transport to or uptake by the nucleus of the host cell.

21. The vector delivery structure of claim 1, wherein the target cell is a human cell.

22. The vector delivery structure of claim 1, wherein the target cell is a pluripotent stem cell.

23. A vector delivery structure for delivering to the interior of a target cell one or more therapeutic nucleotide sequences and one or more proteins that bind to DNA for facilitating the integration of the one or more therapeutic nucleotide sequences into the genome of the host cell, the vector delivery structure comprising:

a) a cochleate comprising a lipid bilayer element wherein the layers of the lipid bilayer element are bound together by a divalent calcium cation;

b) at least one Rep 68 protein and at least one Rep 78 protein of adeno associated virus type II; and

c) a polynucleotide comprising one or more inverted terminal repeat regions of

adeno-associated virus type II and one or more oligonucleotides or polynucleotides, each containing a therapeutic nucleotide sequence that expresses a therapeutically beneficial molecule.

24. The vector delivery structure of claim 23, wherein the polynucleotide is selected from the group consisting of a plasmid or nucleic acid construct.

25. The vector delivery structure of claim 23, wherein, the one or more oligonucleotides or polynucleotides comprise a length of DNA that is flanked at each end by at least one inverted terminal repeat regions.

26. The vector delivery structure of Claim 23, 24 or 25, wherein the structure does not include a polynucleotide that expresses one or more proteins that facilitate integration.

27. The vector delivery structure of claim 23, wherein the target cell is a human cell.

28. The vector delivery structure of claim 23, wherein the target cell is a pluripotent stem cell.

29. A pharmaceutical composition comprising:

a) a vector delivery structure comprising:

- 1) a cochleate comprising a lipid bilayer element and cations;
- 2) one or more proteins that facilitate the integration of one or more therapeutic nucleotide sequences into the genome of a host cell; and
- 3) a polynucleotide comprising one or more DNA sequences recognized by the one or more proteins and one or more oligonucleotides or polynucleotides, each containing a therapeutic nucleotide sequence that expresses a therapeutically beneficial molecule; and

b) a pharmaceutically acceptable carrier.

30. The vector delivery structure of claim 29, wherein the polynucleotide is selected from the group consisting of a plasmid or nucleic acid construct.

31. The pharmaceutical composition of claim 29, wherein the structure does not include a polynucleotide that expresses one or more proteins that facilitate integration.

32. The pharmaceutical composition of claim 29, wherein the cation is a divalent cation.

33. The pharmaceutical composition of claim 29, wherein the cation is calcium.

5 34. The pharmaceutical composition of claim 29, wherein the one or more proteins that facilitate the integration of one or more therapeutic nucleotide sequences into the genome of a host cell is a binding protein that has a DNA binding function.

35. The pharmaceutical composition of claim 34, wherein the one or more binding proteins are from adeno-associated virus type II.

36. The pharmaceutical composition of claim 34, wherein the one or more binding proteins are at least one adeno-associated virus protein selected from the group consisting of Rep 68 and Rep 78.

37. The pharmaceutical composition of claim 34, wherein the one or more binding proteins comprise with Rep 68 and Rep 78.

38. The pharmaceutical composition of claim 29, 36 or 37, wherein the one or more DNA sequences recognized by the one or more binding proteins are the inverted terminal repeat regions of adeno-associated virus.

39. The pharmaceutical composition of claim 38, wherein the one or more oligonucleotides or polynucleotides comprise a length of DNA that is flanked at each end by at least one of the inverted terminal repeat regions.

40. The pharmaceutical composition of claim 34, wherein at least one of the one or more binding proteins is an integrase and at least one of the one or more DNA sequences recognized by the one or more binding proteins is a substrate for said integrase.

41. The vector delivery structure of claim 40, wherein at least one of the one or more binding proteins is an integrase that is not Rep 68 or Rep 78.

42. The vector delivery structure of claim 34, wherein at least one of the one or more binding proteins is a helicase and at least one of the one or more sequences recognized by the one or more DNA binding proteins is a substrate for said helicase.

43. The pharmaceutical composition of claim 34, wherein at least one of the one or more binding proteins is a DNA excision enzyme and at least one of the one or more DNA sequences recognized by the one or more binding proteins is a substrate for said DNA excision enzyme.

44. The pharmaceutical composition of claim 34, wherein at least one of the one or more binding proteins is an isomerase and at least one of the one or more DNA sequences recognized by the one or more binding proteins is a substrate for said isomerase.

45. The pharmaceutical composition of claim 34, wherein at least one of the one or more binding proteins is a telomerase and at least one of the one or more DNA sequences recognized by the one or more binding proteins is a substrate for said telomerase.

46. The pharmaceutical composition of claim 34, wherein at least one of the one or more binding proteins is a DNA repair enzyme and at least one of the one or more DNA sequences recognized by the one or more binding proteins is a substrate for said DNA repair enzyme.

47. The pharmaceutical composition of claim 29, wherein at least one of the one or more proteins that facilitate the integration of the one or more therapeutic nucleotide sequences into the genome of the host cell is a protein that has gene regulatory activity and at least one of the one or more DNA sequences recognized by the one or more binding proteins is a substrate for said protein that has gene regulatory activity.

48. The pharmaceutical composition of claim 29, wherein at least one of the one or

more proteins that facilitate the integration of the one or more therapeutic nucleotide sequences into the genome of the host cell is a protein that facilitates transport to or uptake by the nucleus of the host cell.

49. The pharmaceutical composition of claim 29, wherein the target cell is a human cell.

50. The pharmaceutical composition of claim 29, wherein the target cell is a pluripotent stem cell.

51. A pharmaceutical composition comprising:

a) a vector delivery structure for delivering to the interior of a target cell one or more therapeutic nucleotide sequences and one or more proteins that bind to DNA for facilitating the integration of the one or more therapeutic nucleotide sequences into the genome of the host cell, the vector delivery structure comprising:

1) a cochleate comprising a lipid bilayer element wherein the layers of the lipid bilayer element are bound together by a divalent calcium cation;

2) at least one Rep 68 protein and at least one Rep 78 protein of adeno-associated virus type II; and

3) a polynucleotide comprising one or more inverted terminal repeat regions of adeno-associated virus type II and one or more oligonucleotides or polynucleotides, each containing a therapeutic nucleotide sequence that expresses a therapeutically beneficial molecule; and

b) a pharmaceutically acceptable carrier.

52. The vector delivery structure of claim 51, wherein the polynucleotide is selected from the group consisting of a plasmid or nucleic acid construct.

53. The pharmaceutical composition of claim 51, wherein the one or more

oligonucleotides or polynucleotides comprise a length of DNA that is flanked at each end by at least one inverted terminal repeat regions.

54. The pharmaceutical composition of claim 51, 52 or 53, wherein the structure does not include a polynucleotide that expresses one or more proteins that facilitate integration.

5 55. The vector delivery structure of claim 51, wherein the target cell is a human cell.

56. The vector delivery structure of claim 51, wherein the target cell is a pluripotent stem cell.

57. A method for transforming a target cell with one or more therapeutic nucleotide sequences, the method comprising transfecting a target cell with a vector delivery structure comprising:

10 a) a cochleate comprising a lipid bilayer element and cations;
b) one or more proteins that facilitate the integration of one or more therapeutic nucleotide sequences into the genome of a host cell; and

15 c) a polynucleotide comprising one or more DNA sequences recognized by the one or more proteins and one or more oligonucleotides or polynucleotides, each containing a therapeutic nucleotide sequence that expresses a therapeutically beneficial molecule.

58. The vector delivery structure of claim 57, wherein the polynucleotide is selected from the group consisting of a plasmid or nucleic acid construct.

20 59. The method of Claim 57, wherein the structure does not include a polynucleotide that expresses one or more proteins that facilitate integration.

60. The method of claim 57, wherein the cation is a divalent cation.

61. The method of claim 57, wherein the cation is calcium.

62. The method of claim 57, wherein the one or more proteins that facilitate the

integration of one or more therapeutic nucleotide sequences into the genome of a host cell is a binding protein that has a DNA binding function.

63. The method of claim 62, wherein the one or more binding proteins are from adeno-associated virus type II.

5 64. The method of claim 62, wherein the one or more binding proteins are at least one adeno-associated virus protein selected from the group consisting of Rep 68 and Rep 78.

65. The method of claim 62, wherein the one or more binding proteins comprise both Rep 68 and Rep 78.

66. The method of claim 57, 64 or 65, wherein the one or more DNA sequences recognized by the one or more binding proteins are the inverted terminal repeat regions of adeno-associated virus.

67. The method of claim 66, wherein the one or more oligonucleotides or polynucleotides comprise a length of DNA that is flanked at each end by at least one of the inverted terminal repeat regions.

68,. The method of claim 62, wherein at least one of the one or more binding proteins is an integrase and at least one of the one or more DNA sequences recognized by the one or more binding proteins is a substrate for said integrase.

69. The vector delivery structure of claim 68, wherein at least one of the one or more binding proteins is an integrase that is not Rep 68 or Rep 78.

70. The method of claim 62, wherein at least one of the one or more binding proteins is a helicase and at least one of the one or more DNA sequences recognized by the one or more binding proteins is a substrate for said helicase.

71. The method of claim 62, wherein at least one of the one or more binding proteins is a DNA excision enzyme and at least one of the one or more DNA sequences recognized by the one or more binding proteins is a substrate for said DNA excision enzyme.

72. The method of claim 62, wherein at least one of the one or more binding proteins is an isomerase and at least one of the one or more DNA sequences recognized by the one or more binding proteins is a substrate for said isomerase.

73. The method of claim 62, wherein at least one of the one or more binding proteins is an telomerase and at least one of the one or more DNA sequences recognized by the one or more binding proteins is a substrate for said telomerase.

74. The method of claim 62, wherein at least one of the one or more binding proteins is a DNA repair enzyme and at least one of the one or more DNA sequences recognized by the one or more binding proteins is a substrate for said DNA repair enzyme.

75. The method of claim 57, wherein at least one of the one or more proteins that facilitate the integration of the one or more therapeutic nucleotide sequences into the genome of the host cell is a protein that has gene regulatory activity and at least one of the one or more DNA sequences recognized by the one or more binding proteins is a substrate for said protein that has gene regulatory activity.

76. The method of claim 57, wherein at least one of the one or more proteins that facilitate the integration of the one or more therapeutic nucleotide sequences into the genome of the host cell is a protein that facilitates transport to or uptake by the nucleus of the host cell.

77. The method of claim 57, wherein the target cell is a human cell.

78. The method of claim 57, wherein the target cell is a pluripotent stem cell.

79. The method of claim 57 or 78, performed in the absence of cytokine stimulation.

80. The method of claims 57, wherein the target cells are transfected in culture and are then returned to the same animal or placed in another animal.

81. A method for transforming a target cell with one or more therapeutic nucleotide sequences, the method comprising transfecting a target cell with a vector delivery structure for delivering to the interior of the target cell one or more therapeutic nucleotide sequences and one

or more binding proteins for facilitating the integration of the one or more therapeutic nucleotide sequences into the genome of the host cell, the vector delivery structure comprising:

a) a cochleate comprising a lipid bilayer element, wherein the layers of the lipid bilayer element are bound together by a divalent calcium cation;

5 b) at least one Rep 68 protein and at least one Rep 78 protein of adeno-associated virus type II; and

c) a polynucleotide comprising one or more inverted terminal repeat regions of the adeno-associated virus and one or more oligonucleotides or polynucleotides, each containing a therapeutic nucleotide sequence that expresses a therapeutically beneficial molecule.

10 82. The vector delivery structure of claim 81, wherein the polynucleotide is selected from the group consisting of a plasmid or nucleic acid construct.

83. The method of claim 81, wherein the one or more oligonucleotides or polynucleotides comprise a length of DNA that is flanked at each end by at least one of the inverted terminal repeat regions.

84. The method of claim 81, 82 or 83, wherein the structure does not include a polynucleotide that expresses one or more proteins that facilitates integration.

85. The method of claim 81, wherein the target cell is a human cell.

86. The method of claim 81, wherein the target cell is a pluripotent stem cell.

87. The method of claim 81 or 86, performed in the absence of cytokine stimulation.

88. The method of claim 81, wherein the target cells are transfected in culture and then returned to the same animal or placed in another animal.